

Chapter 4

Economic Evaluation and Its Types

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INTRODUCTION

Economic evaluation is now a widely used technique. In this chapter, we introduce the basics of the approach and discuss how it may be employed in practice. We discuss the various forms of economic evaluation available, which include cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost–benefit analysis (CBA), and cost–utility analysis (CUA). The aim of this chapter is to explain the basic building blocks of these forms of economic evaluation. To achieve this aim, we will pursue the following learning objectives:

1. What is economics and how does it guide how health economists work?
2. What costs should be measured, given a study's chosen perspective?

3. Should health be measured in terms of intermediate or final outcomes?
4. How should outcomes be measured and valued in economic evaluation studies?
5. What are the differences between the different methods of economic evaluation?
6. What is incremental analysis and how should uncertainty be represented?

To begin, let us examine how economists think when undertaking their work.

THE LOGIC OF HEALTH ECONOMICS AND ECONOMIC EVALUATION

Health economists are concerned with analyzing choices about the best use of scarce healthcare resources. Their work is underpinned by the concept of the “health production function” (Fig. 4.1).

As the health production function shows, healthcare interventions may be judged in terms of the costs of their inputs and the value of their outcomes. Health economists evaluate the relative efficiency of competing treatments by comparing their inputs to their outcomes.

Setting the Scene

Before we explain how health economists undertake an economic evaluation, it is useful to ask the question: What is economics? One popular definition states:

Economics is the science which studies human behaviour as a relationship between ends and scarce means which have alternative uses.

Robbins, p. 16 [1]

In this definition, the main elements of economic analysis are included:

1. *Scientific methods*: Economics is based upon the scientific approach of identifying a testable hypothesis, gathering the relevant data, and performing statistical analysis.
2. *Decision-making*: Economics is an aid to decision-making. Economists do not make decisions themselves. They just provide the supporting evidence so decisions may be made.
3. *Alternatives*: Decision-makers must choose between available options. Part of the job of the economist is to identify and to outline the feasible alternatives.

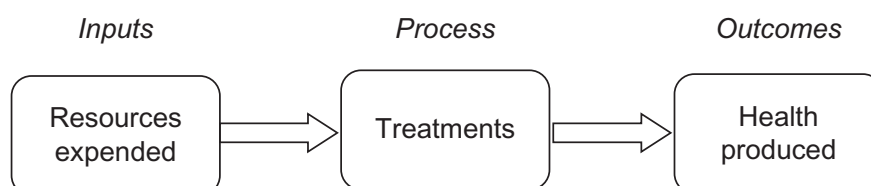


FIGURE 4.1 The health production function.

4. *Efficiency*: Economists must define what is meant by efficiency in a given context and support decision-makers trying to make optimal choices about resource use.
5. *Scarcity*: Resources available to improve patient health are always limited. They should be used in ways that improve efficiency.

ECONOMIC EVALUATION

Economic evaluation generates evidence to guide choices about the allocation of scarce resources. Formally, “economic evaluation” may be defined as:

The comparative analysis of alternative courses of action in terms of both their costs and consequences.

Drummond et al., p. 4 [2]

This definition suggests that a full economic evaluation of healthcare programs must:

- evaluate at least two alternatives, including all relevant options such as “do nothing” or “current practice/usual care,”
- assess both inputs (costs) and outputs (consequences) in terms of resource use and health gain.

When performed properly, economic evaluations provide decision-makers with structured, rigorous evidence for assessing the relative efficiency of competing healthcare interventions. However, best practice suggests that an economic evaluation is best undertaken after the following studies have been performed:

- Studies to assess whether the intervention can work (i.e., its efficacy).
- Studies to assess whether it does any harm (i.e., its safety).
- Studies to assess whether the intervention works in practice (i.e., its effectiveness).

These preliminary studies establish whether an intervention is safe and effective before the economic evaluation is executed. Once this has been established, we can consider conducting the economic evaluation. This will involve two steps: (1) measuring costs and outcomes and (2) combining both costs and outcomes to assess cost-effectiveness. In the next sections, we will cover these steps in detail.

MEASURING COSTS

Costs in economic studies are usually divided into two main types:

Direct costs: These are the costs of resources consumed during treatment. Direct costs can be incurred by social services, healthcare systems, and/or patients. They can be fixed, semi-fixed, or variable [2]. Fixed costs are those generated regardless of the numbers of patients treated. The largest

components of the fixed costs are capital (e.g., buildings and equipment) and overheads (e.g., lighting, heating, and cleaning). Variable costs are those costs that vary with activity. These include any form of intervention or consumables expended during patient care (for instance, drugs, blood products, investigations, and physician time). Finally, semi-fixed costs are those that tend to increase in response to large changes in an activity. Staff costs can be an example of semi-fixed costs (unless they vary directly with activity, when they should be considered as variable costs).

Indirect costs: The biggest component of these costs relates to loss of production due to time off-work which results from illness or its treatment. It is usually referred to as “productivity costs.” The importance of productivity costs is largely dependent on the disease area being considered. When considering diseases affecting working-age groups, indirect costs would be considered an important cost component. Examples include low back pain, asthma, depression, and migraine. Indirect costs are considered less important in diseases of the older age groups because the costs of not working are less. There are two major approaches to valuing indirect costs: (1) the human capital approach and (2) the friction method [3]. The differences between the estimates obtained from the two approaches are more substantial in case of long-term illness or early retirement than in the case of short periods of absence from work. The decision regarding which categories of costs to include in an evaluation depends upon the perspective of the evaluation.

Perspective

When performing an economic evaluation, the perspective taken affects how costs are measured. In formal terms, the “perspective” of an evaluation may be defined as the “view point from which the economic analysis is conducted” [2]. If the viewpoint of the analysis changes, the cost categories included in the analysis should alter. For instance, costs from the perspective of the individual paying privately for care is likely to differ from those from the perspective of the healthcare commissioner paying for care for the whole local population. In standard economic evaluations, the following perspectives are usually considered:

- Societal perspective: where all costs are included.
- Healthcare perspective: includes only the costs of healthcare services.
- Patient perspective: only the costs of services paid for privately by the patient are included.

As this list suggests, the perspective taken should determine how costs are measured. As well as the standard ones listed above, other valid perspectives could include “provider,” “pharmacy,” or “insurance” perspective. Again, these alternatives require measuring costs in different ways and are likely to result in

different estimates of resource use. In most economic evaluations of healthcare programs, only direct costs are considered. The indirect loss to society due to reduced participation in the workforce is usually ignored. The following types of direct costs are usually included in an evaluation:

1. *Health sector costs*: these include resources expended in overheads, staffing, and treatment. For example, pharmacist time, drugs, hospital stay, surgeries, primary care visits, facilities, and administration.
2. *Costs in other sectors*: these include non-healthcare resources. For example, resources expended by social services, criminal justice, and voluntary sector.
3. *Costs to patient/family members*: resources paid for by individuals and their families. For example, travel, child care, out-of-pocket expenses, and carers' time.

The resources consumed in each of these categories are usually identified, measured, and valued. This process involves, first, stating what resources should be included. For instance, doctor and nurse time. Second, measuring patient consumption of units of these different resource types. For instance, the number of hours of a senior doctor's time engaged. Then, the units of resource consumed should be multiplied by weights that reflect national prices for these resources. For instance, an hour of senior doctor time may cost £120 at national pay rates (even though some providers may pay more or less depending upon local market conditions). Costs derived in this manner may not be the same individual commissioners pay for the identified services. Indeed, health economists view costs as *price weighted resource units* rather than *actual spends in actual markets*.

Opportunity Cost

According to many health economists, the resources consumed during patient care should be valued at their "opportunity cost" [4]. The opportunity cost of choosing one alternative over another is the benefits sacrificed by not pursuing the next best alternative. For instance, the cost of providing a drug utilization review for one patient should be judged in terms of the health gain sacrificed by other patients who, as a result, cannot have their medicine regimes examined. In other words, the resources used for one purpose cannot be used for another. In a health context, examples of "opportunity cost" are many. For example, opting to fund more surgeries eliminates the resources available for preventative interventions. The opportunity cost of funding one heart bypass operation could be the benefits lost from (for example) providing 100 vaccinations for Measles, Mumps, and Rubella. In this example, unvaccinated children pay for the bypass operation in terms of their lost health.

Time Horizon

When capturing the costs and benefits of an intervention, economic evaluations must account for differences in resource use and health gain over time. For instance, some interventions may have an instant, profound effect, which soon tails off. Others may have a smaller impact that lasts for longer. Therefore, economic evaluators must decide how long the costs and the outcomes of an intervention should be tracked? In other words, they must choose the “time horizon,” which is defined as the “length of time over which costs and consequences are assessed.” As a guiding principle, the time horizon of an evaluation should be long enough to capture significant differences in costs and consequences between the interventions being compared. If the chosen time horizon does not reflect the observed pattern of costs and consequences, then the results of an economic evaluation are likely to be unreliable. Therefore, choosing the correct time horizon is vital to a study’s success. If the length of a trial is too short and fails to capture the full costs and the full benefits of an intervention, health economists call this situation “censoring” because important data has been suppressed by poor study design.

Discounting

Because resources have different values now compared to the future, the costs and benefits should be “discounted.” Resources and outcomes that accrue beyond the first year should be discounted to their “net present value.” Making future costs and consequences reflect their current value in this way ensures that studies reflect “positive time preference.” This refers to our preference as individuals to consume benefits now but pay for them later [4]. In most studies, the “discount rate” is usually set between 0% and 6%. In the United Kingdom, for instance, the chosen discount rate is often 3.5%, which is based upon Treasury guidelines. Studies that fail to discount both costs and benefits will be seen as failing to meet the required standards for economic analysis.

MEASURING OUTCOMES

The outcomes used in economic evaluations should ideally reflect final health outcomes rather than intermediate clinical markers. This is in contrast to clinical practice, where the focus is usually on measuring intermediate physiological indicators. It is usually straightforward to decide on a final outcome measure for acute conditions, as interventions are usually curative (e.g., the use of antibiotics to cure respiratory tract infections). For chronic conditions, the use of intermediate indicators is more prevalent. If intermediate markers are used, this should be on the basis that they are surrogates for final outcomes. For example, the level of glycated hemoglobin (HbA1c) is a

diabetes outcome that has a validated link to overall health and quality of life. Importantly, the choice of an outcome defines the type of the economic evaluation that may be employed. Therefore, we will describe the different outcomes that can be used in economic evaluations because the choice of outcomes measured will determine the type of studies performed.

Physiological Measures and Clinical Events

Physiological measures are disease-specific outcome measures. Physiological measures such as cholesterol levels, blood pressure (BP), and bone density are widely used in clinical practice. The link between such measures and clinical events has been widely accepted in the clinical community. For example, high BP is known to be a risk factor for stroke. The availability of such data allows intermediate outcomes to be reliably used in economic evaluations of interventions designed to prevent undesirable clinical events. [Fig. 4.2](#) illustrates this concept.

Risk functions estimate the risk of clinical events as a function of the level of the physiological measure; controlling for other epidemiological factors such as age, gender, race, etc. This allows an economic evaluation to be undertaken to assess the cost-effectiveness of using the intervention to reduce the risk of an unwanted event. However, the ultimate aim is not only to avoid these events but to avoid their “consequences” in terms of disability or death. Therefore, intermediate outcomes do not capture the final outcome—i.e., health—that patients wish to improve or maintain. Therefore, generic measures of health such as survival or quality of life (QoL) are usually preferred.

Survival

Survival data are usually collected in randomized controlled trials (RCTs). They are normally expressed as the proportion of patients alive at the end of

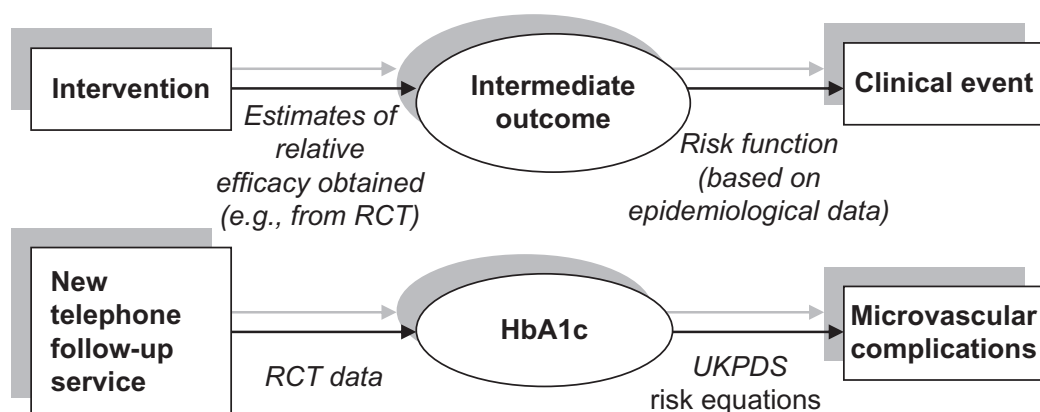


FIGURE 4.2 Linking intermediate to final outcomes. *UKPDS*, UK Prospective Diabetes Study; *RCTs*, randomized clinical trials.

a trial, the number of deaths averted, or (more commonly) the number of life years saved (LYS). As clinical trials may only last for a short period of time, extrapolating beyond the trial period might be needed to assess longer term outcomes.

Quality of Life

When evaluating interventions aimed at reducing the burden of chronic diseases, the primary objective may not be improving survival but rather improving patient functioning in terms of mental state and physical abilities. Therefore, outcome measures must be able to capture improvements across these dimensions. Within health economics, QoL measures have been developed that can complete this task of capturing health-related quality of life (HRQoL). Such measures usually follow the World Health Organization (WHO) definition of “health” being a “combination of physical, mental and social wellbeing, not merely the absence of disease” [5].

Measures of HRQoL can either be generic or disease specific [6]. Disease-specific measures focus on dimensions of the patient QoL related to a particular condition. For example, the Beck Depression Inventory (BDI) and the Multiple Sclerosis Quality of Life Inventory (MSQLI). These measures have the advantage of being more sensitive to the impact of particular diseases. However, they cannot be used for decision-making regarding the allocation of resources across more than one condition. For instance, the BDI cannot be used to compare outcomes measured with, for instance, the MSQLI. In comparison, generic measures of HRQoL do not focus on particular diseases but rather on the general dimensions of health such as depression, pain, mobility, etc. These measures are less sensitive to changes in patient disease status. Commonly used versions of this class of instruments include the Short Form-36, the Nottingham Health Profile, the Sickness Impact Profile, and the General Wellbeing Scale.

Utility

Utility is another generic measure that can be used to compare outcomes across different patient groups and disease areas. It may be defined as the “value a person places on a particular health state or health outcome” [6]. This valuation will differ from one person to another. Therefore, individuals can value different health states based on their own preferences. Usually, the utility scale ranges from 0 (the value attached to being dead) to 1 (the value attached to being in full health). Utility values can also be negative, when a health state is valued as being worse than death.

In economic evaluations, utility data are usually collected using “off-the-shelf” questionnaires that have: (1) a descriptive system that outlines the various health states and (2) an accompanying “tariff” with utility values

attached to each health state. An example of a preference-based, prescored generic measure is the Euroqol-5D. This is one of the most widely used of such measures (see <http://www.euroqol.org/>).

As well as off-the-shelf valuation systems, it is possible to elicit health state preferences directly using a direct valuation technique designed to elicit preferences. Two stages are involved in the process of direct elicitation: (1) describing the health state to the individual, then (2) eliciting their preference for being in this particular health state. The simplest method of eliciting preferences and measuring values is through the use of a rating scale such as the Visual Analogue Scale (VAS). As Fig. 4.3 illustrates, participants in a study can be asked to indicate where on the VAS their current health state (or a health state described to them) should be recorded.

Although informative, the values obtained using VAS are not utilities because they do not involve making a choice, between alternatives. In economic evaluation studies, the preferred methods for measuring utilities are the Standard Gamble (SG) or the Time Trade-Off (TTO) methods [2].

The SG method is the one preferred by health economists because it is based on making choices and taking risks. The method involves offering respondents two alternatives:

1. The first alternative has two possible outcomes which are: (1) living in full health (with probability p) or (2) immediate death (with probability $1-p$).
2. The second alternative has one certain outcome of living in the health state you are valuing, “ h ,” as a chronic condition, for the remaining years of life.

The interviewer varies the probability p until the respondent is indifferent between the two alternatives. At this point, the utility attached to the chronic health state, h , is considered to be equivalent to p . This is calculated by assigning a utility value of 0 to death and 1 to being in full health. At the point of indifference, the utility of the first alternative ($1 \cdot p + 0 \cdot [1 - p] = p$) is equivalent to the utility of the second alternative (utility of health state “ h ”). Fig. 4.4 illustrates a classic SG.

In the TTO method, the respondent is offered two alternatives:

1. Alternative 1 is full health for time “ X ” (where $X < t$) followed by death.
2. Alternative 2 is to remain in health state “ h ” for time t (life expectancy the condition of interest) followed by death.

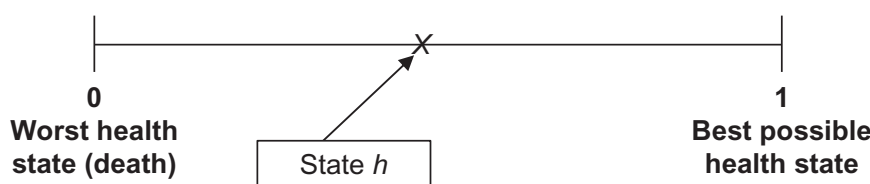


FIGURE 4.3 Example of VAS.

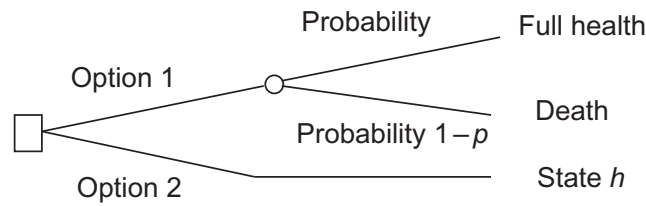


FIGURE 4.4 SG method.

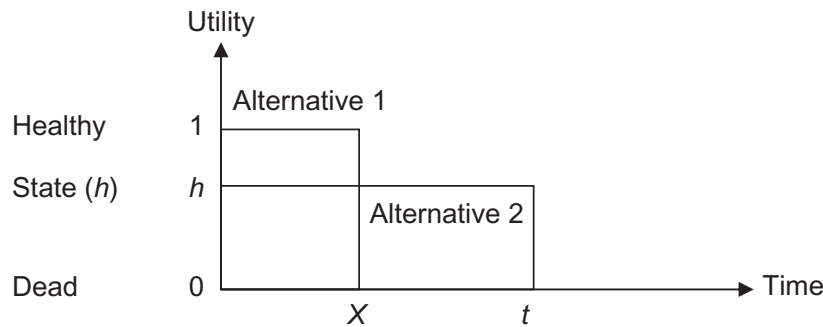


FIGURE 4.5 TTO method.

In this approach, X is varied until the respondent is indifferent between the two alternatives. At the indifference point, the utility of state “ h ” is given by X/t . At the point of indifference, the following holds:

$$\text{Utility of full health (1)} * X = \text{Utility of state } h * t$$

Therefore,

$$\text{Utility of state } h = X/t$$

Fig. 4.5 illustrates the TTO method.

Quality-Adjusted Survival

Given the importance of both survival and QoL, the use of an outcome measure that encompasses both is preferable. The quality-adjusted life year (QALY) is a generic outcome measure that captures both length of life (i.e., survival) and QoL (expressed in terms of utilities). For example, 1 year lived in full health is equal to $1 * 1 = 1$ QALY. In contrast, 1 year lived with 0.5 utility is $1 * 0.5 = 0.5$ QALY.

The QALY is a preferred measure for many healthcare decision-makers because it can be used for comparisons across different diseases. Alternative measures include the healthy years equivalent (HYE) and the disability-adjusted life year (DALY). These alternative measures are often used outside economic evaluation studies. For instance, DALYs have been used in international comparisons by the WHO to estimate the burden of disease [7].

Monetary Outcomes

It is also possible to express the outcomes of interventions in terms of individual or society willingness to pay for specific outcomes. Two possible approaches to valuing health outcomes in money terms are [8]:

- *The human capital approach*: where earnings are used as a measure of health benefit. For example, if one intervention allows an individual to remain in work for a greater number of years than another, the difference in earnings is used to estimate the money value of the differential health gain.
- *The willingness to pay approach*: an individual's willingness to pay for a particular amount of health gain is used to approximate its monetary value. This technique is also called Contingent Valuation. It seeks to elicit how much an individual would be willing to pay to avoid an illness or particular side effects, or to receive a specific set of health benefits.

COMBINING COSTS AND OUTCOMES USING INCREMENTAL ANALYSIS

Economic evaluation is not concerned with the absolute values of costs and outcomes. For instance, knowing that a single intervention A has a cost of £12,000 and a gain of 0.5 QALYs does not help decision-makers because this information includes no comparison. Therefore, most economic evaluations compare the cost-effectiveness of an intervention with one (or more) alternative(s). To do so, an incremental cost-effectiveness ratio (ICER) is calculated. As Eq. (4.1) shows, the mean cost (C_i) and mean effect (E_i) for each intervention is calculated and compared as follows:

$$\text{ICER} = \frac{C_B - C_A}{E_B - E_A} \quad (4.1)$$

The ICER values are usually presented graphically on a cost-effectiveness plane (Fig. 4.6), where the “anchor point” is provided by the costs and effects for intervention A. In this diagram, effects are presented on the X-axis and costs on the Y-axis. Hence, any intervention that appears higher than A will have higher costs. Similarly, any intervention that appears below will be cheaper. On the effects side, any intervention that exists to the right of A will have higher benefits. Any intervention to the left will produce lower benefits. The slope of the line connecting interventions A and B is equal to the ICER of B versus A.

The results of the comparison of B versus A can appear in any of the four quadrants. In the South East quadrant, the new intervention (B) is more effective and less costly than the comparator (A) and is said to be “dominant.” Therefore, cost-effectiveness is automatically demonstrated. In the North West quadrant, the new intervention is more costly and less

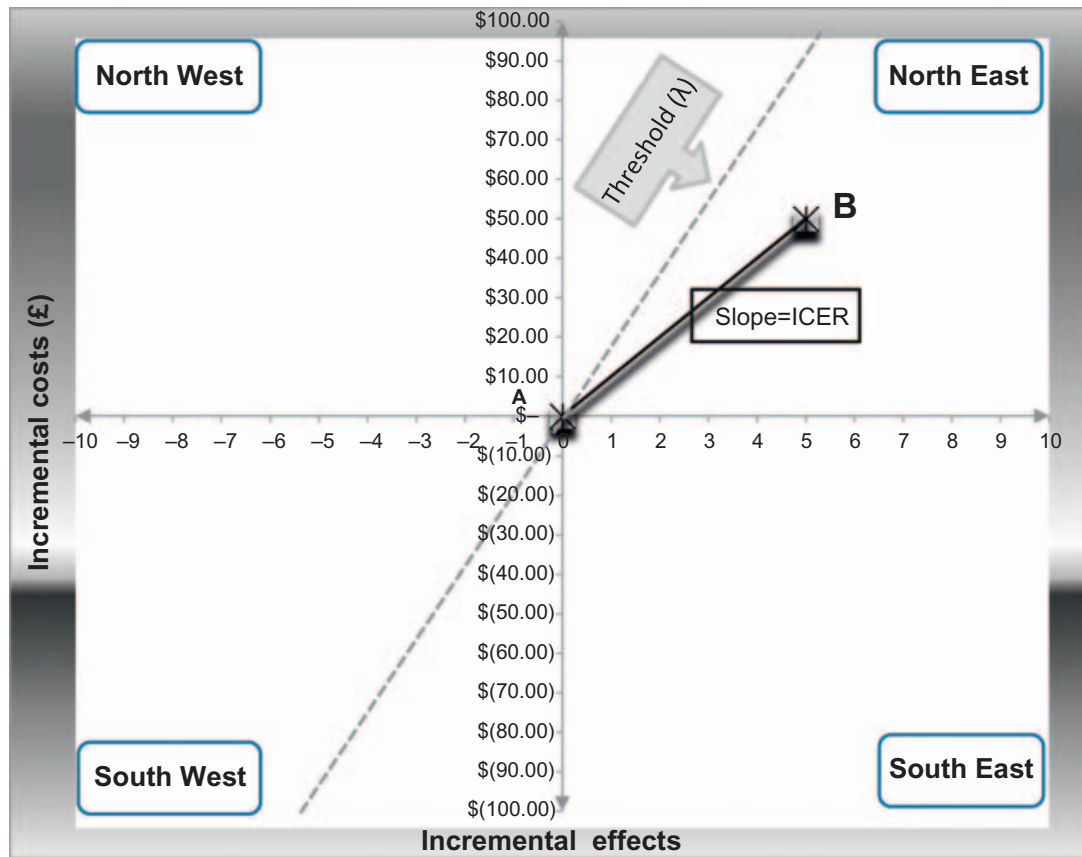


FIGURE 4.6 Cost-effectiveness plane and the cost-effectiveness threshold.

effective, so is “dominated” by the comparator (A). Hence, the intervention is not cost-effective. In the North East and South West quadrants, the new intervention is either more effective but more costly or less effective and less costly. In both cases, further consideration will be required to assess whether the gain in outcomes is worth the extra cost. This requires setting a willingness-to-pay or cost-effectiveness threshold (denoted by λ) for the decision-maker.

Although the ICER is a popular analytical tool, the use of a ratio in analyzing cost-effectiveness data can be problematic. In particular, ratios can be unstable at extreme values. Also, the ICER formula is often unable to differentiate between identical coordinates with positive and negative values such as $(-1, -2)$ compared to $(1, 2)$. Stinnett and Mullahy [9] examined the problems of the ICER and proposed an alternative measure based upon average net health benefits (NHBs).

$$\text{NHB}_A = E_A - C_A/\lambda \quad (4.2)$$

As Eq. (4.2) shows, the average NHB of intervention A may be calculated by taking the difference between average effects and average costs for intervention A, and using the threshold (λ) as a weighting that converts costs into effects. This approach solves the problems associated with the ICER. Using the

NHB approach, two interventions may be compared. The incremental NHB (INHB) of intervention B versus intervention A is:

$$\text{INHB}_{BA} = (E_B - E_A) - [(C_B - C_A)/\lambda] \quad (4.3)$$

As this formula suggests, incremental cost-effectiveness can be calculated in terms of NHBs. The first part of the equation ($E_B - E_A$) represents the difference in health benefits produced by the two interventions. The second part $(C_B - C_A)/\lambda$ represents the health gain that could have been produced if incremental costs were converted into health gain at the rate given by lambda (λ). Therefore, the total formula gives the incremental net health gain produced by the comparative technologies and may be used in healthcare decision-making. Similarly, Net Monetary Benefit (NMB) can be calculated and compared between interventions, by calculating incremental NMB.

DECISION RULES

Economic evaluations are performed to provide information for decision-makers. By themselves, health economists do not make choices about the allocation of scarce resources. Consequently, the analyst must know what “decision rule” will be employed by decision-makers in making resource allocation decisions. For instance, choosing interventions that maximize clinical effectiveness is a possible decision rule. The decision rule usually chosen by health economists is dominance in terms of incremental cost-effectiveness. In other words, any intervention that has a “dominant” or superior ICER relative to its competitors should be chosen. In all forms of economic analysis, information is constructed to support the use of a specific decision rule.

For instance, the ICER may be used as a decision rule to establish dominance. To support the analysis, societal values may be included in the form of a value for the cost-effectiveness threshold. In absence of clear dominance, societal cost-effectiveness thresholds create a decision rule which stipulates that any intervention with an ICER below the threshold value should be funded. In contrast, any intervention with an ICER above the required threshold should not be adopted for use. In other words, any intervention with incremental costs and effects lying to the right of the threshold illustrated in [Fig. 4.6](#) should be adopted.

Assessing Uncertainty

Although the ICER, NHBs and other tools have been developed to aid decision-makers, they are based on average or mean values of costs and effects. While incremental differences in average cost-effectiveness are important, point estimates of economic values fail to take account of any uncertainty surrounding the results. As most studies are sampling unknown

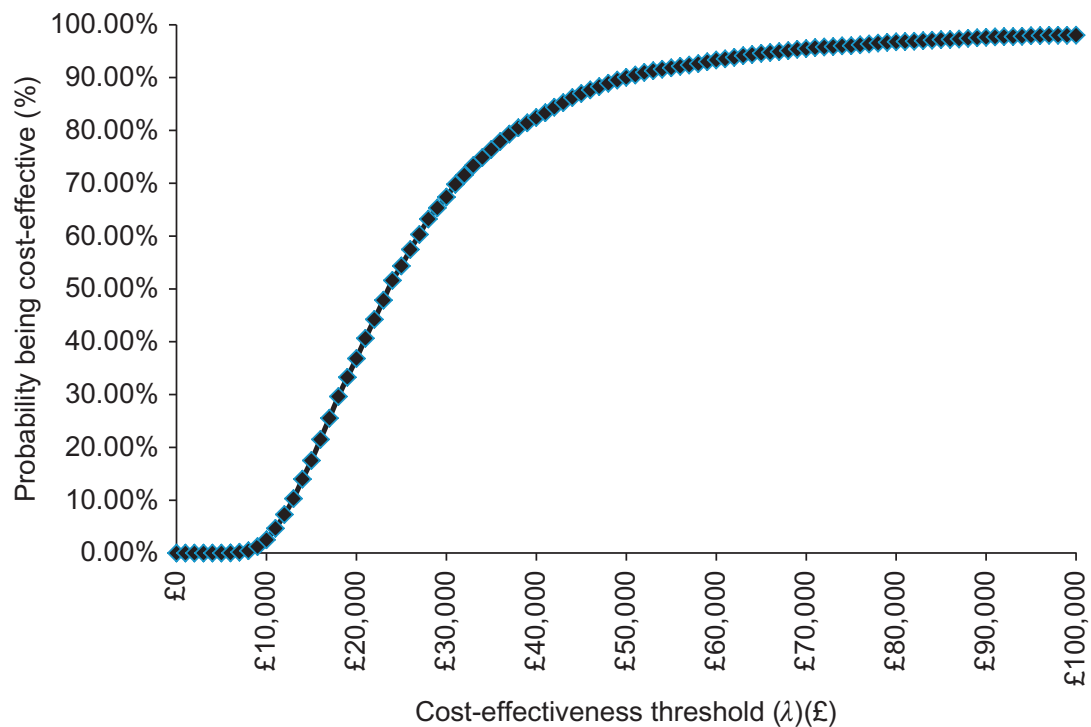


FIGURE 4.7 Cost-effectiveness acceptability curve.

population data, the mean value sampled could vary in future sampling. Therefore, there is “uncertainty” in the cost-effectiveness estimates that studies produce. In response, confidence intervals (CIs) could be fitted around the mean values of ICER and NHB calculations. As fitting CIs can be problematic, many health economists use the cost-effectiveness acceptability curve (CEAC) to represent uncertainty in the joint distribution of costs and benefits [10]. The CEAC is constructed by plotting the proportion of cost and effect pairs that are cost-effective for a given range of “ λ ” (Fig. 4.7). The construction process starts by calculating this proportion when the slope is zero (i.e., equivalent to the X -axis). Then the process is continuously repeated for increasing values of “ λ ”.

In health economic analysis, the CEAC indicates the probability that an intervention is cost-effective compared with its alternative, given the observed cost and effects, under different values of “ λ .” The CEAC presents the probability that an intervention is cost-effective, given different degrees of uncertainty. The decision to adopt a technology should not be based solely upon the CEAC. The results of the main analysis using ICERs or NHBs should be the main driver of adoption decisions. Using the CEAC as the means of deciding whether to recommend a treatment or not is a common mistake and should be avoided. The CEAC can only represent uncertainty, the diagram cannot tell decision-makers which technology to adopt. Choices about adoption must be based upon the point estimates of analysis such as an incremental NHB calculation.

TYPES OF ECONOMIC EVALUATIONS

In all types of economic evaluation, costs are measured in the same way. So, the type of evaluation performed is largely determined by the type of outcomes that studies wish to capture. The following are the main types of economic evaluation, with a comparison of the outcomes they measure:

- CMA: where outcomes are assumed to be equal.
- CEA: where outcomes are measured as natural/physical units.
- CUA: where outcomes are measured using a generic measure such as the QALY.
- CBA: where benefits are expressed in monetary terms.

Below, we introduce these main types of economic evaluations and give examples of their use in evaluating pharmacy/pharmacist-delivered services.

Cost-Minimization Analysis

The use of CMA requires evidence that the interventions compared are identical in terms of outcomes. If this is the case, then only costs are compared. The term “comparative cost analysis” is sometimes used to describe this type of analysis. The assumption of equivalence in outcomes is a very strong one to make, given that comparators are unlikely to be completely identical in their effects. An example of a CMA study is comparing the cost of administering the same medication in different settings. For example, home administration of antibiotics for cystic fibrosis compared with inpatient treatment. Another example is the comparison of a proprietary drug with its generic equivalent. To be valid, CMA requires outcomes to be 100% equivalent in such studies. However, it is easy to see how home administration could produce different health outcomes than inpatient treatment. Similarly, generics may not be clinically equivalent to their reference standards. In such instances, CMA is a partial rather than a full economic evaluation. In response, many health technology assessment agencies across the world are reluctant to accept economic evaluations of this type as evidence of value for money [11]. [Box 4.1](#) includes some examples of studies that used CMA to evaluate pharmacy and pharmacist services.

Cost-Effectiveness Analysis

In a CEA, outcomes are measured using natural units (e.g., number of symptom free days, strokes avoided, and life years gained). Intermediate outcomes can also be used (reduction in BP (mmHg) or reduction in blood glucose levels), if they can be linked to health outcomes. A single outcome measure is used in cost-effectiveness studies. If more than one outcome is considered, the evaluation is considered to be a cost-consequences analysis (CCA). Using CEA, it is not possible to compare different clinical areas that do not have the same primary outcome. CEA does not allow studies to

BOX 4.1 Examples of CMA

Armour et al. [12] compared the costs of a pharmacy-based central intravenous additive service (CIVAS) with those of traditional ward-based preparation of intravenous doses for a pediatric population. The analysis involved comparing the costs of labor, disposables, and diluents as well as the costs avoided as a result of using part-vials in CIVAS.

Data were collected for 20 CIVAS sessions (501 doses) and 26 ward-based sessions (30 doses). The results showed that the pharmacy-based CIVAS was cost saving ($p < 0.001$). Sensitivity analysis was conducted to test the robustness of the results to assumptions relating to the skill-mix. This showed that the cost saving was maintained over a full range of skill mixes.

Scott et al. [13] conducted a CMA alongside multicenter RCT of a community pharmacy medication management service (MEDMAN) in the United Kingdom with 12-month follow-up. The sample size was 1480 (980 intervention and 500 control). The intervention involved initial consultation at study start, with further consultations based on pharmacist-determined need. Significant differences were not found in any of the clinical outcomes including appropriate medications as defined by the National Service Framework and self-reported medication compliance. This was given as the rationale for using a CMA rather than a CEA, although the point estimate showed improvement in QoL. Comparing costs only showed that total cost for intervention subjects was higher, controlling for baseline differences ($p = 0.001$).

Perraudin et al. [14] compared home-based subcutaneous immunoglobulin (SCIg) therapy to hospital-based intravenous infusions (IVIg) with support from a multidisciplinary team including a pharmacist from a societal perspective in Switzerland. The study follow-up was 3 years. The program provided long-term support from self-administration training to the responsible use of therapy (proper adherence, optimal efficacy, and safety). The authors report that over the short term, additional costs from purchasing equipment and the drug therapy management program were offset by avoiding hospital costs.

combine more than one measure of outcome. For example, impact on quantity and quality of life cannot be considered at the same time (Box 4.2).

Cost–Utility Analysis

In CUA, outcomes are assessed using generic measures such as the QALYs. CUA is sometimes considered a special type of CEA, and some researchers use the terms interchangeably. CUA has two main advantages over other forms of economic evaluation. First, it uses measures that combine length and quality-of-life. Second, the use of a standardized, generic measure enables economic comparisons across different disease areas with very different clinical outcomes. Consequently, decision-makers, such as the UK's NICE, prefer this method because it facilitates choices about budget allocation across the whole spectrum of disease areas (Box 4.3).

BOX 4.2 Examples of CEA and CCA

Polgreen et al. [15] reported the results of a CEA conducted alongside a clinical trial (The Collaboration Among Pharmacist and Physicians to Improve Blood Pressure Now trial). The aim was to assess the cost-effectiveness of physician–pharmacist collaboration to improve hypertension control. The outcomes in the trial were the reduction in systolic and diastolic BP and proportion of patients with controlled BP. The costs included were those of medications and pharmacist and physician time. The results were reported in terms of the cost per unit reduction in BP. These showed that the collaborative intervention achieved better control of BP (average systolic BP was 6.1 mmHg lower (± 3.5), diastolic was 2.9 mmHg lower (± 1.9)) but had higher costs (a difference of \$202.93). This means that the cost to lower BP by 1 mmHg was \$33.27 for systolic BP and \$69.98 for diastolic BP. The authors concluded that this collaborative service was cost-effective.

Elliot et al. [16] conducted a CEA alongside a RCT of a community pharmacy-based service, for patients prescribed new medication, compared to usual care. Patients were aged 75 years or older or suffering from stroke, cardiovascular disease, asthma, diabetes or rheumatoid arthritis, and on four or more medications. The intervention consisted of two community pharmacists trained using the self-regulatory model theory delivered intervention consisting of a telephone call to the patient 2 weeks after recruitment to enquire about how they were getting on with their medication using a semi-structured interview format. The main outcome measure was patient adherence to medication. The authors reported improvement in adherence to newly prescribed medication in the intervention group (89% vs 81%) in addition to cost saving compared to usual care (£188 vs £283 vs mean total costs per patient).

Desborough et al. [17] conducted a CCA of the Norfolk Medicines Support Service which was an adherence focused, pharmacist-led medication review service provided by community pharmacists. Patients 65 years or older and registered with a GP in Norfolk, residing in their own home, were referred to the service by anyone in their care that identified they were having difficulties managing their medication. The main health outcomes assessed in the study were HRQoL and adherence. Service provision, prescribing, and secondary care costs were considered. The results showed that the intervention reduced emergency hospital admissions and increased medication adherence but no significant change in HRQoL was observed. The costs of providing this medication review service were offset by the reduction in emergency hospital admissions and savings in medication cost, with a saving in the mean total cost per patient of £307 (95% CI: £1296–£655).

Lalonde et al. [18] conducted a CCA to evaluate pharmacist follow-up of patients receiving anticoagulants compared to normal physician follow-up. The outcomes assessed included quality of international normalized ratio (INR) control, incidence of complications, HRQoL, use of healthcare services. The study was a RCT. The results showed that pharmacist-managed patients have seen their family physician less often (95% CI -3.1 to -0.1 visits per year). Number of INR tests, incidence of complications, and HRQoL were similar in both groups. The incremental cost of the follow-up service was estimated at CAN\$123.80 per patient year.

BOX 4.3 Examples of CUA

Sullivan et al. [19] evaluated the lifetime costs and benefits of managing warfarin therapy to prevent strokes in elderly patients with atrial fibrillation. They compared usual care versus anticoagulation management services, where dedicated anticoagulation professionals monitor and oversee patients. The analysis was conducted from a societal perspective. Health outcomes were measured in terms of QALYs gained. Utility values were based on a large national survey. Costs were expressed in US\$ and included drugs (such as warfarin and aspirin), INR monitoring, lab and imaging investigations, clinic visits, and resource use associated with major bleeding and treatment of primary events. The results were improved effectiveness by a mean of 0.057 QALYs and reduced costs by a mean of US\$2100 saving (2004 values) compared with usual care. The study suggests that anticoagulation clinic management was dominant (i.e., more effective and less costly) compared to usual care.

The RESPECT trial team [20] conducted a CUA to evaluate the provision of medication reviews in community pharmacists. The intervention was provided by pharmacists who received training that covered the theory and practice of pharmaceutical care, practical exercises in collaborating with the GPs. Training took place just before the start of each 12 months period. Forty-five practices and 62 community pharmacists participated in the study. The primary outcome assessed in this evaluation was QALYs-gained. The results showed the intervention to be more costly (incremental cost: £192; 95% CI: –£150 to £579) and more effective (incremental QALYs: 0.019; 95% CI: –0.023 to 0.102) with an ICER of £10,000 per QALY gained. Thus, the intervention was considered to be cost-effective, where the ICER is less than the UK NICE cost-effectiveness threshold of £20,000 to £30,000 per QALY-gained.

Wallerstedt et al. [21] conducted a CUA alongside a RCT to assess the cost-effectiveness of a clinical pharmacist service at two internal medicine wards at a university hospital in Sweden. The intervention was a composite in-hospital clinical pharmacist service (medication reviews, drug treatment discussion with the patient at discharge, and a medication report). The main health outcome in the economic evaluation was the number of QALYs gained. The results showed that although the intervention patients gained an additional 0.0035 QALYs on average, with an incremental cost of €1622 per patient, the intervention was not considered to be cost-effective as this resulted in an ICER of €463,371 per adjusted QALY gained. The probabilistic uncertainty analysis revealed that, at a willingness-to-pay threshold of €50,000/QALY, the probability that the intervention was cost-effective was approximately 20%.

Cost–Benefit Analysis

In CBA, outcomes are valued in monetary terms, where money values are attached to the health states resulting from the interventions being compared. To be considered a CBA, formal assessment of willingness to pay for the outcomes should be undertaken using recognized elicitation methods.

Formal methods for eliciting preferences may measure either stated or revealed preferences [22]. These methods include conjoint analysis using Discrete Choice Experiments. CBA is useful for the allocation of resources on the macro-level (e.g., allocating funding across healthcare programs) because it gives a net return on investment that can be compared across all programs. In CBA, a societal perspective is used for costing. However, CBA is rarely used in healthcare evaluations due to the lack of acceptability of assigning monetary value to health outcomes and the majority of the studies that claim to be a CBA are in reality not considered to be so.

SUMMARY

In this chapter, we introduced the theoretical basis of economic evaluation. We introduced the building blocks required for conducting economic evaluation studies, namely: measuring costs and outcomes. We also explained how decision rules may be used in judging cost-effectiveness and how decision-makers may use them to reach decisions regarding the adoption of new interventions. Finally, we discussed the different types of economic evaluations and gave examples of their use in the evaluation of pharmacy services.

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